## Remarks/Argument

Claim 32 is pending in the application and has been amended. Support for amended Claim 32 is found on page 7, first paragraph of the Specification. This Amendment complies with 35 U.S.C. 112, 1st paragraph since the Specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed; *i.e.* a transgenic knock-out mouse comprising a specific disruption of the gene encoding a potassium transport channel comprising SEQ ID NO:5. No new matter has been added by this amendment.

Response to the section 112, 1st paragraph enablement rejection

Claim 32 has been rejected under 35 U.S.C. 112, 1st paragraph as allegedly being non-enabled because the claim does not recite a specific phenotype for the transgenic TASK knock-out mouse. According to pg. 4 of the Office Action, "without a phenotype, either in the claim or in the Specification, the skilled artisan will not know how to use the claimed mouse because it fails to differ from any wild-type mouse".

As discussed in the Specification at page 28, lines 12-18, the claimed transgenetic animals "enable the preparation of live models for studying animal diseases associated with the TASK family of channels".

Thus, the Office Action apparently considers that this use of the claimed transgenic mice as a live model requires the identification of a specific phenotype, which differs from the wild-type animal, in order to study diseases associated with the TASK potassium channel without undue experimentation.

We respectfully disagree with this requirement that a specific phenotype must be identified in order to use the claimed transgenic mice as a model of channel diseases. One skilled in the art can, without more, readily use the claimed transgenic mice for this purpose.

One purpose of the invention disclosed in the Applicants' Specification is associated with the cloning of the TASK channel, and corresponds to the identification of specific and high affinity pharmacological agents that block these channels. Thus, the Specification teaches one of ordinary skill in the art that the "cloning of TASK, … should help to … identify specific and high affinity pharmacological agents that would block these channels …".

In view of this purpose, and as discussed in the Specification, "The discovery of this new member of potassium channels and the cloning of the new member of this family provides, notably, new means for screening drugs capable of modulating the activity of these new potassium channels, and thus of preventing or treating the diseases in which these channels are involved." See pg. 3, lines 20-23 of Applicants' Specification.

One way that screening for such drugs can be accomplished is through the use of the claimed transgenic knock-out mice, whose genome comprises a disruption of a gene encoding the potassium channel comprising SEQ ID NO: 5. Such mice can readily be used as a means for screening and identifying specific and high affinity pharmacological agents that would block this channel using only routine techniques.

For example, in order to identify such pharmacological agents, one can first screen for substances that are capable of modulating the activity of the TASK-1 channel *in vitro* in cells expressing this channel. This step is clearly described in the Specification on page 27, line 23 to page 28, line 11.

After positive TASK-1 specific pharmacological agents are identified by *in vitro* assay, such agents can be administered to wild-type animals for the identification of potential pharmacological agents to treat channel diseases, and then to the claimed transgenic animals (which do not express TASK-1 channel) in order to select the potential pharmacological agents which are specific to TASK-1. In this step, these transgenic animals can constitute a control for the TASK-1 specificity of the identified potential pharmacological agents.

Thus, the transgenic animals of the invention effectively correspond to a new means for screening drugs capable of modulating the activity of TASK-1 new potassium channels, which drugs can prevent or treat the diseases in which these channels are involved.

As stated above, this use of the claimed transgenic animals does not necessitate any undue experimentation by one skilled in the art, but rather employs only routine experiments. In fact, this use requires only the absence of TASK-1 expression in the transgenic animals, and no specific phenotype has to be identified for them. Indeed, the phenotype may not become apparent until after the mouse is treated with agents that block TASK-1 activity. The identification of a phenotype for the claimed transgenic mice in this manner can therefore be a desired outcome of the screening process, which belies the need to identify a specific phenotype before the claimed mouse is used.

The fact that no specific phenotype must be identified for such a use of the claimed transgenic animals is confirmed by the abstract of Linden *et al.*, which was submitted with the Amendment dated February 4, 2005. In this abstract, the authors were looking for compounds that modulated the activity of TASK-1. To this end, they compared the effect of the administration of different anesthetic compounds to wild-type and TASK-1 knock-out mice, when no phenotype had been previously identified for these transgenic mice. Clearly, those of

skill in the art are able to use the claimed transgenic mice without undue experimentation, even when the mouse phenotype is unknown.

In conclusion, the Specification contains ample teaching how to use the claimed transgenic mice. The guidance provided in the Specification regarding how to use the claimed mice is not undue, as Linden et al. shows that only routine experiments are needed. Claim 32 is thus enabled, and the rejection under 35 U.S.C. 112, 1st paragraph should be withdrawn.

Claim 32 has also been rejected under 35 U.S.C. 112, 1st paragraph as allegedly not enabling for the full breadth of the genus of TASK-1 genes which have been knocked-out. According to pg. 6 of the Office Action, "the claim broadly encompass(es) knocking out any gene that indirectly causes a deficiency in the expression of the potassium transport channel comprising SEQ ID NO:5".

The amended Claim 32 is now directed to "a transgenic knock-out mouse, whose genome comprises a disruption of the gene encoding a potassium transport channel comprising SEQ ID NO:5, which is deficient in the expression of said potassium transport channel". Consequently, Claim 32 as amended is directed to encompass TASK-1 knock-out genes that directly cause a deficiency in the expression of said potassium transport channel.

The Office Action states on pg. 6, third paragraph, that SEQ ID NO: 5 is not a complete polypeptide sequence, and thus does not represent a polypeptide normally expressed in mice. The Office Action thus alleges that "the skilled artisan would not know how to find or disrupt a genomic locus encoding the claimed ***non-existing*** protein" (emphasis added). As shown in Figs. 8A and 8B, the partial amino acid sequence of SEQ ID NO: 5 represents all but three amino acids of the full-length mouse TASK-1. One skilled in the art can readily use the virtually full-length sequence presented in SEQ ID NO: 5 to identify and disrupt the endogenous TASK-1

mouse locus, using only routine experimentation. Indeed, the authors of the Linden et al. reference did just that, producing a transgenic mouse that falls within the scope of the claims by following the teachings of the Applicants' Specification.

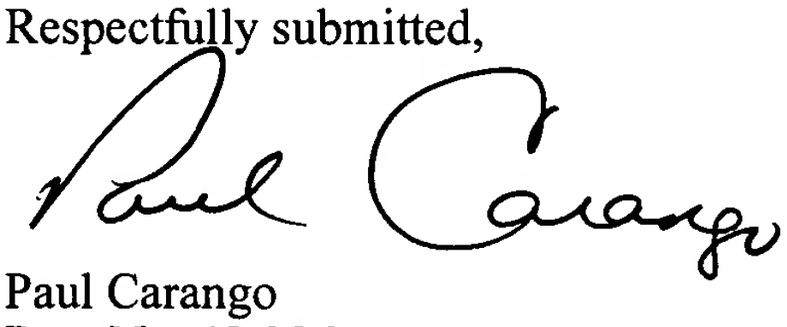
Finally, Claim 32 has also been rejected under 35 U.S.C. 112, 1st paragraph as allegedly being non-enabled for chimeric transgenic animals. According to pg. 6 of the Office Action, "the Claim 32 as written encompasses chimeric mice (genetic mosaics) wherein only a portion of the cells of the mouse comprises the claimed genetic disruption".

As suggested by the Examiner, the amended Claim 32 is now directed to "a transgenic knock-out mouse whose genome comprises a disruption of the gene encoding a potassium transport channel comprising SEQ ID NO:5, which is deficient in the expression of said potassium transport channel". The Applicants submit that, in view of this change, Claim 32 is now enabled.

In light of the foregoing, the Applicants respectfully request withdrawal of the 35 U.S.C. 112, 1st paragraph rejection.

The Applicants respectfully submit that the entire Application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,



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